LUTONIX DRUG COATED BALLOON PTA CATHETER FOR TREATMENT OF STENOTIC OR OBSTRUCTIVE LESIONS IN THE FEMOROPOPLITEAL ARTERY

POST-APPROVAL STUDY PLAN

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1 Background

Early in the IDE Submission review process for the Lutonix DCB, FDA had identified the need for Lutonix to collect additional safety data beyond what would be available from the IDE pivotal study and per the following future considerations requested that Lutonix develop a plan for collecting the additional safety data to detect rare adverse events:

> *"It is unclear if your IDE clinical study alone will provide sufficient information to detect rare adverse events (i.e., those that occur at a 1 - 2% rate). Given the high-risk nature of percutaneous vascular interventions, the added risks of both the drug and the device, and the first-of-a-kind nature of this technology, the ability to detect many types of adverse events with increased precision will be important both for FDA review and advisory panel input. With these considerations in mind, FDA believes that your overall clinical assessment of the Moxy Drug Coated Balloon should incorporate a statistically powered evaluation of rare adverse events using an appropriate number of subjects.*
>
> *Please establish a plan for collecting and providing this safety information, discuss the individual adverse event rates expected for this population as well as for this type of combination product, and discuss how your proposed overall sample size can detect clinically significant differences in adverse events. Additional enrollment into the US trial, separate registry studies (for populations that would not be included in the pivotal trial, such as patients with certain risk factors), a continued access study, or a combination thereof are all potential options to achieve this study population minimum. In addition, the overall safety evaluation should allow for each of the proposed balloon sizes to be adequately represented in the overall sample. Global experience with this product, particularly from prospectively defined studies or registries, may also assist with your safety assessment."*

Given FDA's request and given that the intent of the post-approval study regulation is for collection of additional clinical safety data beyond what may be necessary at the time of the pre-market approval, Lutonix initiated the post-approval type safety registry studies (LEVANT 2 Continued Access and LEVANT 2 Safety Registry) with intent to satisfy both the desire for additional clinical data at the time of the panel meeting and the anticipated requirement for additional clinical safety data as condition of approval per 21 CFR 814.82(a)(2).

The post-market type safety registries together have enrolled an additional 657 Lutonix drug coated balloon (DCB) patients beyond the 372 DCB patients enrolled as part of the LEVANT 2 Randomized pivotal study (for total of 1029 Lutonix DCB patients), all with follow-up scheduled out to 5 years.

In addition to the above studies, Lutonix has also completed the LEVANT 1 randomized trial and enrollment into the Lutonix Global SFA registry is in process. Together, these 5 studies will have enrolled total of over 2000 Lutonix DCB patients with the same intended use (treatment of SFA) as the pre-market application and will provided significant amount of clinical data for evaluation of long term safety and efficacy of the Lutonix DCB.

Summary of the respective trials is provided in the table below. Outline of the post-market type safety registries protocol (LEVANT 2 Continued Access/LEVANT 2 Safety Registry) is provided in **Section 2**.

Table 1. Lutonix Femoropopliteal Clinical Studies

Study	Description	Patient Enrollment	Misc
LEVANT I Randomized Study	European Study, Randomized 1:1 (DCB vs. POBA).	n= 101 patients (49 DCB vs. 52 POBA)	Final report completed (2-year follow-up).
Lutonix 2 Randomized (Pivotal IDE Study)	Pivotal Study, Randomized 2:1 (DCB vs. POBA)	n= 543 patients enrolled: 56 roll-in, 476 rand (316 DCB v. 160 POBA), 11 standard practice.	12m interim report completed. 5-yr follow-up planned.
Lutonix 2 Continued Access/Safety Registry	Safety Registry Study	n= 657 DCB patients	Enrollment completed. Follow-up in process. 5-yr follow-up planned.
Lutonix Global SFA Registry	Safety Registry Study	Up to 1000 patients	Enrollment and follow-up in process. 2 yrs follow-up planned. Patients consented to 5-yrs.

In conclusion, the totality of clinical data (over 2000 Lutonix DCB patients) that will be collected in these five studies - LEVANT 1 Randomized trial, LEVANT 2 Randomized trial (pivotal IDE study), LEVANT 2 Continued Access Registry, LEVANT 2 Safety Registry and the Lutonix Global SFA Registry - is sufficient to assess the continued long term safety and effectiveness of the Lutonix DCB as intended per the post-approval study regulation per the FDA Amendment Act of 2007.

2 Post-Approval Study Plan

The addition of the LEVANT 2 Continued Access registry and the LEVANT 2 Safety registry studies together were intended to fulfill the need for additional clinical data to assess the continued long term safety and effectiveness of the Lutonix DCB as intended per FDA Amendment Act of 2007.

The study protocol for the LEVANT 2 Continued Access registry and the LEVANT 2 Safety registry studies are the same. Per regulation, separate 'Continued Access' protocol was necessary for continued enrollment at the same US clinical sites as the pivotal IDE study and as separate 'Safety' protocol was necessary for enrollment at new US clinical sites.

The post-approval study outline for the LEVANT 2 registry studies is provided below.

As the LEVANT 2 registry studies themselves should be sufficient to fulfill the requirement of the post-approval study requirements, the post-approval study timeline and reporting requirement are based on the LEVANT 2 registry studies timeline.

The Lutonix Global SFA registry study is also supportive of the continued long term safety and effectiveness of the Lutonix DCB. The reporting of the Global SFA Registry data and analyses will be provided as additional supporting evidence, in coordination with reports from the LEVANT 2 pivotal and LEVANT 2 registry studies, of device safety and efficacy.

2.1 Background

The purpose of the LEVANT 2 registry studies is to collect additional safety and efficacy information on the Lutonix Drug Coated Balloon for treatment of stenosis or occlusion of the femoropopliteal arteries in a larger patient population. Enrolled subjects will meet the same protocol requirements and undergo the same follow up and testing schedule as the LEVANT 2 Randomized pivotal study.

The enrollment in the LEVANT 2 registry studies were completed on 30 Sept 2013. The studies enrolled the same patient population and followed the same medication regimen, follow-up schedule, and definitions as the LEVANT 2 Randomized pivotal study. Total of 657 Lutonix DCB patients were enrolled from total of 63 sites across the US and Europe. These patients will be followed at 1, 6, 12, 24, 36, 48 and 60 months. The primary endpoint is rate of unanticipated device- or drug-related adverse events over time through 60 months.

2.1.1 Device Description

The Lutonix Drug Coated Balloon is a standard PTA catheter with a drug coating on the balloon portion of the catheter. The Lutonix Drug Coated Balloon is an over-the-wire type design with working lengths of 100 and 130 cm and is compatible with 0.035" guidewires. Marker bands are located at the proximal and distal ends of the balloons to assist in delivery and placement. The balloon surface between the marker bands is coated with a specialized immediate release non-polymer based coating formulation that includes the anti-proliferative drug – paclitaxel - at a surface concentration of 2µg/mm^2.

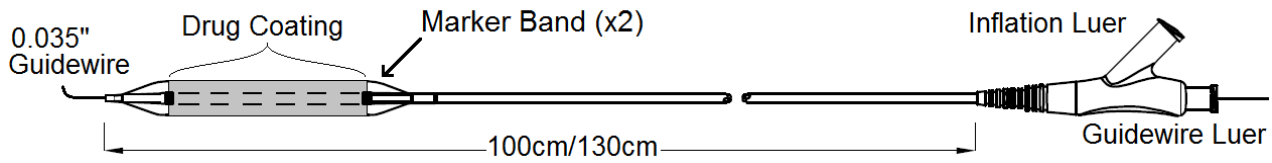


Figure 1: Lutonix Drug Coated Balloon

All devices are provided sterile and for single-use only and are clearly labeled for investigational use only.

2.1.2 Intended Use

The Lutonix Drug Coated Balloon is indicated for percutaneous transluminal angioplasty of obstructive de novo or non-stented restenotic lesions in native femoropopliteal arteries ≤15cm in length and ≥4.0 to ≤6.0mm in diameter.

2.1.3 Regulatory History

The Lutonix 035 Drug Coated Balloon PTA Catheter has only been approved for Investigational use only in the USA.

The Lutonix 035 Drug Coated Balloon PTA Catheter is commercially available outside of the US, including Europe and other countries, for use in treatment of lower limb vascular disease.

2.2 Objectives

The primary objective of the LEVANT 2 registry studies is to assess safety and efficacy of use of the Lutonix Drug Coated Balloon for treatment of stenosis of the femoropopliteal arteries in a large population of subjects.

The data from the all LEVANT 2 DCB test subjects (roll-in, randomized, and registries) will be used to reconfirm the superior efficacy at 24 months and the data from the LEVANT 2 registry studies will be used to reconfirm the non-inferior of safety at 12 months as compared to the PTA control results from the LEVANT 2 Randomized (pivotal) study.

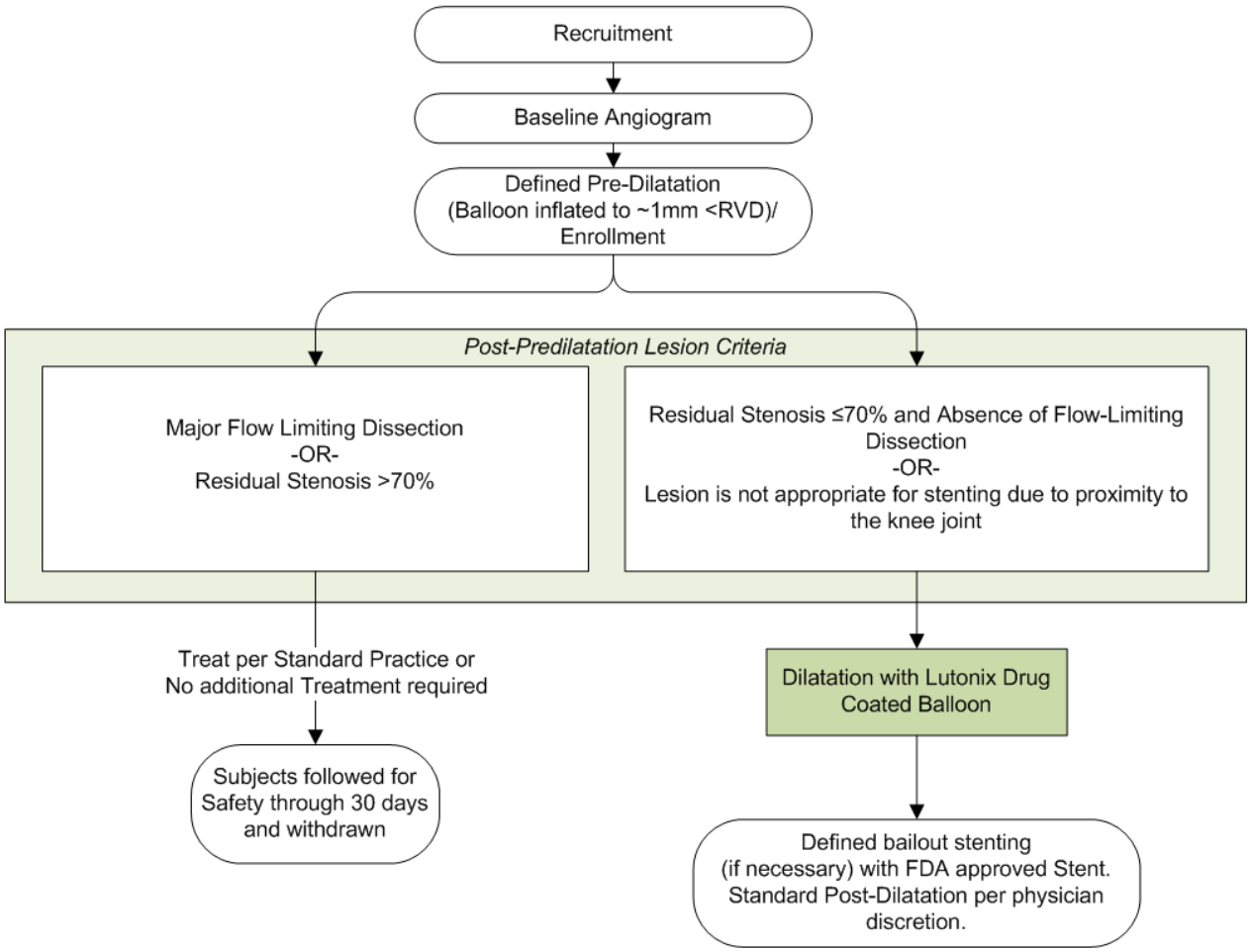
Additionally, the data from the LEVANT 2 registry studies will be combined with the DCB patients from the LEVANT 2 Randomized study to assess for safety of rare adverse events.

2.3 Study Design

The study will enroll subjects presenting with claudication or ischemic rest pain and an angiographically significant lesion in the superficial femoral or popliteal artery and a patent outflow artery to the foot. After successful protocol-defined pre-dilatation, subjects that are unlikely to require a stent based on strict angiographic criteria (absence of major flow-limiting dissection from the lumen and ≤ 70% residual stenosis or the lesion is not appropriate for stenting due to proximity to the knee joint) will be treated with the Lutonix Drug Coated Balloon.

Subjects that do not meet post-predilatation criteria are excluded (and treated per standard practice) and followed for safety only (via telephone or clinical follow up) for 30 days. Treated subjects will have ultrasound and clinical follow-up through 2 years and telephone follow-up through 5 years.

Figure 2: Study Flowchart



2.4 Patient Inclusion/Exclusion Criteria

2.4.1 Inclusion Criteria

Subjects must meet all inclusion criteria to be enrolled in the study.

Clinical Criteria

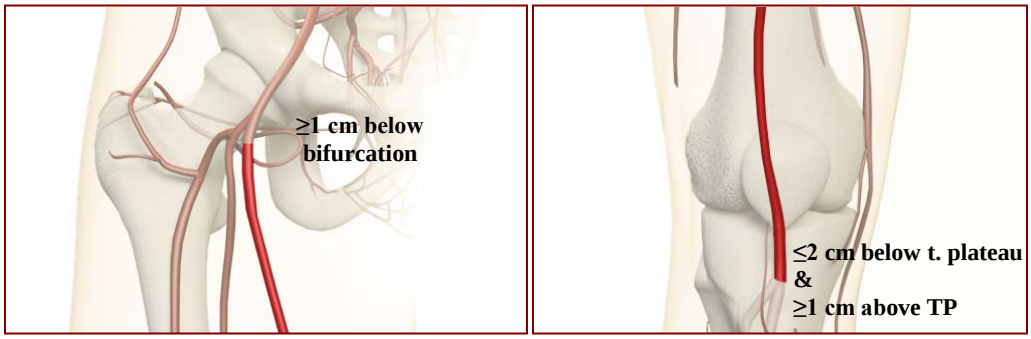
1. Male or non-pregnant female ≥18 years of age;
2. Rutherford Clinical Category 2-4;

3. Patient is willing to provide informed consent, is geographically stable and comply with the required follow up visits, testing schedule and medication regimen;

Angiographic Criteria - Lesion Criteria

4. Length ≤15 cm;
5. Up to two focal lesions or segments within the designated 15 cm length of vessel may be treated (e.g. two discrete segments, separated by several cm, but both falling within a composite length of ≤15 cm);
6. ≥70% stenosis by visual estimate;
7. Lesion location starts ≥1 cm below the common femoral bifurcation and terminates distally ≤2 cm below the tibial plateau AND ≥1 cm above the origin of the TP trunk;

Figure 3: Allowed Lesion Location



8. *de novo* lesion(s) or non-stented restenotic lesion(s) >90 days from prior angioplasty procedure;
9. Lesion is located at least 3 cm from any stent, if target vessel was previously stented;
10. Target vessel diameter between ≥4 and ≤6 mm and able to be treated with available device size matrix;
11. Successful, uncomplicated (without use of a crossing device) antegrade wire crossing of lesion;
12. A patent inflow artery free from significant lesion (≥50% stenosis) as confirmed by angiography (treatment of target lesion acceptable after successful treatment of inflow artery lesions);

    NOTE: Successful inflow artery treatment is defined as attainment of residual diameter stenosis ≤30% without death or major vascular complication.

13. At least one patent native outflow artery to the ankle, free from significant (≥50%) stenosis as confirmed by angiography that has not previously been revascularized (treatment of outflow disease is NOT permitted during the index procedure);
14. Contralateral limb lesion(s) cannot be treated within 2 weeks before and/or planned 30 days after the protocol treatment in order to avoid confounding complications;
15. No other prior vascular interventions within 2 weeks before and/or planned 30 days after the protocol treatment.

2.4.2 Exclusion Criteria

Patients will be excluded if ANY of the following conditions apply:

1. Pregnant or planning on becoming pregnant or men intending to father children;
2. Life expectancy of <5 years;
3. Patient is currently participating in an investigational drug or other device study or previously enrolled in this study;
   NOTE: Enrollment in another clinical trial during the follow up period is not allowed.
4. History of hemorrhagic stroke within 3 months;
5. Previous or planned surgical or interventional procedure within 2 weeks before or within 30 days after the index procedure;
6. History of MI, thrombolysis or angina within 2 weeks of enrollment;
7. Rutherford Class 0, 1, 5 or 6;
8. Renal failure or chronic kidney disease with MDRD GFR ≤30 ml/min per 1.73 m^2 (or serum creatinine ≥2.5 mg/L within 30 days of index procedure or treated with dialysis);
9. Prior vascular surgery of the index limb, with the exception of remote common femoral patch angioplasty separated by at least 2 cm from the target lesion;
10. Inability to take required study medications or allergy to contrast that cannot be adequately managed with pre- and post-procedure medication;
11. Anticipated use of IIb/IIIa inhibitor prior to randomization;
12. Ipsilateral retrograde access;
13. Composite lesion length is >15 cm or there is no normal proximal arterial segment in which duplex flow velocity can be measured;
14. Significant inflow disease. Successful treatment of inflow disease allowed prior to target lesion treatment;
15. Known inadequate distal outflow (>50% stenosis of distal popliteal and/or all three tibial vessels), or planned future treatment of vascular disease distal to the target lesion;
16. Sudden symptom onset, acute vessel occlusion, or acute or sub-acute thrombus in target vessel;
17. Severe calcification that renders the lesion undilatable;
18. Use of adjunctive primary treatment modalities (i.e. laser, atherectomy, cryoplasty, scoring/cutting balloon, etc.).

2.5 Sample Size Calculation

Based on hypothesis testing of efficacy endpoint at 24 months (all LEVANT 2 DCB test vs. LEVANT 2 Randomized PTA control) and safety endpoint of freedom from composite safety at 12 months (LEVANT 2 Continued Access DCB test vs. LEVANT 2 Randomized PTA control), the post-approval study efficacy dataset consists of all LEVANT 2 DCB test (n=1029; 56-roll-in, 316-randomized and 657-registry) and the safety endpoint dataset consists of the LEVANT 2

registry DCB test (n=657). Given that the sample size for the post-approval study dataset is larger than the sample size of DCB treated subjects from the pivotal study (n=316), the methodology of the pivotal study sample size calculations still apply; the larger sample size will provide additional power for the hypothesis tests.

For assessment of rare adverse events, the planned sample size of 650 of LEVANT 2 registry subjects was based on the following.

Taken together with the LEVANT 2 Randomized pivotal study, the 650 additional combined DCB subjects enrolled in the LEVANT 2 registry studies will provide a safety dataset on 1022 subjects treated with the Lutonix Drug Coated Balloon.

Allowing for up to 15% loss-to-follow-up, an evaluable sample size of 869 test subjects is expected. If the observed rare adverse event rate is 1%, then the upper limit of the 95% Confidence Interval is 1.8% (PASS2008: Exact Clopper-Pearson). Assuming an expected 1% incidence rate, Power is > 95% to observe at least 4 unexpected SAEs (PASS2008: Post-Marketing Surveillance). Similarly, if the observed rate is 2%, then the upper limit of the 95% Confidence Interval is 3.0%. Assuming an expected 2% incidence rate, Power is > 95% to observe at least 11 unexpected SAEs. This study provides the ability to detect and describe the rate of rare unanticipated adverse events with some precision.

2.6 Recruitment Strategy

Enrollment has been completed for the LEVANT 2 registry studies. Total of 657 patients have been enrolled into the LEVANT 2 registry studies (total of 650 was planned).

There were total of 80 sites in these studies - 54 sites from the pivotal study (42 in USA and 12 in Europe) and 26 additional clinical sites (11 in USA and 15 in Europe). Actual enrollment occurred from total of 63 clinical sites.

2.7 Data collection: Study Endpoints

2.7.1 Primary Endpoints

Rate of unanticipated device- or drug- related adverse events over time through 60 months.

2.7.2 Secondary Endpoints

The following endpoints will be reported using descriptive statistics in the final Study Report.

Safety

- Composite of freedom from all-cause perioperative (≤ 30 day) death and freedom from the following at 1, 6, 12, 24, 36, 48, and 60 months: index limb amputation, index limb re-intervention, and index-limb-related death.
- Freedom at 30 days from all-cause death, index limb amputation above the ankle and target vessel revascularization (TVR) (VIVA Safety Endpoint)

The following endpoints will be assessed at 1, 6, 12, 24, 36, 48 and 60 months:

- Rate of unanticipated device- or drug-related adverse events

- All-cause death
- Amputation (above the ankle)-Free Survival (AFS)
- Target Vessel Revascularization (TVR)
- Reintervention for treatment of thrombosis of the target vessel or embolization to its distal vasculature
- Major vascular complications
- Readmission for cardiovascular events

Efficacy

- Acute Device, Technical and Procedural success

The following endpoints will be assessed at 6, 12 and 24 Months:

- Primary and Secondary Patency. Primary Patency is defined as the absence of target lesion restenosis (as adjudicated by blinded core-lab) and freedom from target lesion revascularization (TLR).
- Alternative Primary and Secondary Patency based on alternative definitions of DUS PSVR < 2.0, < 2.5, and < 3.0
- DUS Clinical Patency (target lesion restenosis as adjudicated by blinded core-lab without prior Clinically Driven TLR)
- Target Lesion Revascularization (TLR)
  1. Clinically-driven
  2. Total (clinical and DUS/angiography-driven)
- Change of Rutherford classification from baseline
- Change of resting Ankle Brachial Index (ABI) from baseline

2.8 Follow-up Schedule & Plan to minimize loss to Follow-up

Table 2 displays the required schedule for subject treatment and evaluation. This schedule is consistent with standard clinical care pre- and post-interventional procedures. The times for each test are broad enough to fit into most hospital routine testing procedures.

Subjects enrolled, and treated per standard practice will be followed for safety through 30 days. The 30 day follow-up visit can be performed as a telephone or clinical visit. Duplex ultrasound imaging is not a protocol requirement for this group. Details of each testing requirement can be found in the sections below.

Table 2: Follow-Up Schedule and Testing Requirements for treated subjects

Event	Screening (pre-consent)	Pre-Procedure	Procedure	Post- Procedure	1 Month[1]	6 Month	12 Month	24 Month	36 Month[1]	48 Month[1]	60 Month[1]
Visit Window	30 days	30 days			±2 weeks	±1 month	±1 month	±2 month	±2 month	±2 month	±2 month

Inclusion/Exclusion Criteria	√	√	√								
Informed Consent		√									
Medical History	√										
Physical Exam[2]		√		√	√[3]	√	√	√			
Medication Compliance		√			√	√	√	√	√	√	√
Resting ABI		√[4]		√[4]	√[4]	√	√	√			
Rutherford Classification		√				√	√	√			
Blood Analysis (CBC with differential; BMP, pregnancy[6])		√[5]		√	√[3]	√	√				
Angiogram			√								
Adverse Event Monitoring			√	√	√	√	√	√	√	√	√
Duplex Ultrasound (after clinical assessment)				√[7]		√	√	√			

[1] *Follow-up can be by telephone or clinical visit, depending on timing of duplex ultrasound (if required)*
[2] *Physical Exam must be performed by and MD, PA, or NP*
[3] *Required if clinical visit occurs*
[4] *Resting ABI is required within 90 days of index procedure. Resting ABI is not required post procedure or at 1-month, but investigator encouraged to capture if possible*
[5] *Pre-procedure blood analysis must be performed within 30 days of the procedure*
[6] *Pre-procedure and females of childbearing potential only*
[7] *Baseline duplex is only required once (anytime post-procedure through the 1-month visit)*

At 6, 12, and 24 month follow-up visits, the clinical status of the subject (for assessment of clinical and safety endpoints) should be established prior to performing the required DUS (for assessment of patency).

The Investigator or Research Coordinator will contact treated subjects via phone (or via clinical visit if preferred or as part of a regular follow-up) at approximately 1 month, 36 months, 48 months and 60 months (and possibly longer if required) in order to assess for any adverse events and medication compliance.

All treated subjects will return for follow-up at 1 (if required for duplex ultrasound), 6, 12 and 24 months post procedure. See **Table 2** for required testing at each follow-up visit time point. Following randomization, all subjects are required to complete all assigned follow-up visits and procedures. During the duration of the study, all events need to be reported in the web-based eCRF. Subjects will be instructed to report adverse events to their study physician between evaluation visits.

Relevant medications will be recorded on the eCRF. Anti-platelet therapy compliance including dose, periods of interruption (and reason for interruption), and invasive procedures deterred due to the need to take anti-platelet therapy will also be recorded on the eCRF.

To minimize the lost to follow-up, sponsor will communicate on quarterly basis (at minimum) with the clinical sites to reiterate the importance of follow-up and remind the sites of their particular follow-up patients.

In addition, if a visit is missed, the site is required to document a minimum of three (3) attempts to contact the subject within the follow-up window. If the subject only misses one protocol required visit, the site should repeat the three (3) attempts to contact the subject followed by a certified letter. Only when a subject misses two (2) consecutive follow-up visits with failure of all contact attempts, the subject may then be considered lost to follow up and exited from the study.

2.9 Statistical Analysis Plan

The purpose of the LEVANT 2 registry studies is to collect additional safety and efficacy information of the Lutonix Drug Coated Balloon for treatment of stenosis or occlusion of the femoral and popliteal arteries in a large population of subjects. The LEVANT 2 registry studies are an open-label registry study of the Lutonix Drug Coated Balloon.

Total of 657 subjects were treated with the Lutonix Drug Coated Balloon after successful predilatation.

The Primary Endpoint is the rate of unanticipated device- or drug- related adverse events over time through 60 months. Secondary endpoints include the rate at 1, 6, 24, 36, 48, and 60 months and the primary and majority of the secondary endpoints of the LEVANT 2 Randomized pivotal study as shown above.

Data from all the subjects treated with DCB in the LEVANT 2 Randomized protocol (roll-in and randomized to DCB) and the LEVANT 2 registry studies will be combined and analyzed using descriptive statistics. To assess the consistency of results under different analyses, secondary as-treated (AT) and per-protocol (PP) analyses will be performed for the primary and secondary endpoints. An additional supportive analysis of patients with and without bailout stenting will also be performed based on descriptive statistics, and data will further be presented for PP analysis of subjects with and without bailout stenting. Poolability by geography and by test group (LEVANT 2 Randomized Study roll-ins subjects, randomized subjects in the LEVANT 2 Randomized trial, LEVANT 2 Safety Registry subjects and LEVANT 2 Continued Access Registry subjects) will also be evaluated.

In addition to the primary endpoint, the following secondary endpoints will be hypothesis tested. All other secondary endpoints will be analyzed using descriptive statistics.

2.9.1 Effectiveness Endpoint – Primary Patency at 12 months

Primary Patency is defined as the absence of target lesion restenosis (as adjudicated by blinded core-lab) and freedom from target lesion revascularization (TLR).

2.9.1.1 Statistical Hypothesis

H_0: The proportion of combined LEVANT 2 DCB test subjects (roll-in, randomized, and CA registry) free from efficacy events through 24 months post-index procedure is equal to that from the LEVANT 2 Randomized PTA control group.

H_1: The proportion of all combined LEVANT 2 DCB test subjects free from efficacy events through 24 months post-index procedure is not equal to that from the LEVANT 2 Randomized PTA control group.

$$\mathbf{H_0: P_{CONTROL} = P_{TEST}} \quad \textbf{vs.} \quad \mathbf{H_1: P_{CONTROL} \neq P_{TEST}}$$

Core lab adjudicated target lesion restenosis and CEC adjudicated target lesion revascularization (TLR) are 'efficacy events'.

2.9.1.2 Efficacy Analysis

The statistical analysis will be an asymptotic likelihood ratio chi-square test for inequality of binomial proportions; the test will be a one-sided test at α=0.025. The response variable in each subject will be the presence or absence of at least one efficacy event from the time following the index procedure through 24 months. The primary analysis will be ITT, and a significant rejection of the null hypothesis with results in favor of the Test group will indicate success for this endpoint.

2.9.2 Safety Endpoint – Freedom from composite safety at 12 months

Freedom of composite safety defined as composite of freedom from all-cause perioperative (≤ 30 day) death and freedom from the following at 12 months: index limb amputation, index limb re-intervention, and index-limb-related death.

2.9.3 Statistical Hypothesis

H_0: The proportion of subjects with safety events in the LEVANT 2 Continued Access/Safety group (test) through 12-months post-index procedure is clinically inferior to that of the LEVANT 2 Randomized PTA Control group.

H_1: The proportion of subjects with safety events in the LEVANT 2 Continued Access/Safety group through 12-months post-index procedure is clinically non-inferior to that of the LEVANT 2 PTA Control group.

$$\mathbf{H_0: P_{TEST} - P_{CONTROL} \geq \delta} \quad \textbf{vs.} \quad \mathbf{H_1: P_{TEST} - P_{CONTROL} < \delta^{**}}$$

All-cause perioperative (≤30 day) death, CEC adjudicated index limb amputation (above and below the ankle), CEC adjudicated index limb re-intervention, and CEC-adjudicated index-limb-related death are 'safety events'. ****δ** is the range of differences that is considered not clinically important (it also known as the "range of indifference" or the "margin of noninferiority"). For this analysis, δ=10%.

2.9.4 Safety Analysis

The statistical analysis will be a Farrington & Manning test for non-inferiority of proportions; the test will be a one-sided test at α=0.025. The response variable in each subject will be the presence or absence of at least one safety event from the time following the index procedure through 12 months.

2.10 Study Timeline and Reporting Requirement

Enrollment in the LEVANT 2 registry studies began on June 19, 2012 and was completed on September 27, 2013. Total of 657 subjects were enrolled at 63 sites across the United States (US) and Europe (EU).

Based on the completion of enrollment on Sept 2013, the anticipated follow-up schedule for the respective time points are shown in the table below.

Table 3. LEVANT 2 Registry Studies Follow-Up Schedule

Follow-up	Last Patient Follow-Up	Anticipated Interim and Final Report
Enrollment	Sept 2013	NA
6 Month	March 2014	June 2014
12 Month	Sept 2014	Dec 2014
24 Month	Sept 2015	Dec 2015
36 Month	Sept 2016	Dec 2016
48 Month	Sept 2017	Dec 2017
60 Month	Sept 2018	Dec 2018 (Final Report)

Enrollment for the Lutonix Global Safety Registry was initiated on Dec 11, 2012 from total maximum of 75 clinical sites in Europe. Enrollment to date is 750 patients of the 1000 patients planned. Based on the current enrollment rate and study sites, the enrollment is anticipated to be completed near August of 2014.

While the Global SFA registry study is also supportive of the continued long term safety and effectiveness of the Lutonix DCB, the post-approval requirement is primarily fulfill by the LEVANT 2 registry studies. As such descriptive statistics only will be provided for the Global Registry subjects and no formal hypothesis tests are planned as part of the post-approval study requirements. Reporting of the Global Safety Registry data will be in coordination with reporting schedule as outlined for the LEVANT 2 registry studies show in the table above.